reversible encephalopathy syndrome within 50 days post transplantation, all of them showed complete clinical and radiological resolution. **Conclusion:** Non-myeloablative HSCT using this conditioning regimen for high risk pediatric patients with benign hematological disorders appears to be promising and worth further study.

214

PERICARDIAL EFFUSION (PEF) IS A MAJOR INDEPENDENT RISK FACTOR ASSOCIATED WITH A SIGNIFICANT DECREASE IN SURVIVAL IN PEDIATRIC STEM CELL TRANSPLANTATION (SCT) RECIPIENTS

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Background: SCT is the treatment of choice for a variety of pediatric conditions. Potential post SCT morbidities include cardiac toxicity. Rhodes et al (BMT 2005) reported that PEF was seen in 4.4% of pediatric SCT recipients. Risk factors for the development of PEF have been thought to include GVHD, infection and/or underlying disease. There is a paucity of information regarding the etiology, prognosis, treatment and outcome of PEF in a large cohort of pediatric SCT recipients. **Objectives:** To assess the incidence, risk factors, outcome of PEF and the impact of PEF on overall survival (OS) in pediatric SCT recipients. **Method:** Echocardiograms were performed at baseline prior to 200 SCT (4 were ineligible for review) in 156 patients and when patients had symptoms and/or signs of cardiac or pericardial disease post SCT. Probability of and time to PEF were analyzed by Kaplan-Meier method and risk of PEF and death were determined by multivariate analysis. Covariates included age, gender, ethnicity, conditioning regimen, risk status (CIBMTR criteria), conditioning regimen, donor source, CMV status, GVHD, and HLA match. **Results:** The mean age was 8.15 years (+/- 6.25 years) with 88 males and 68 females. 102 patients received allogeneic transplants, 34 of them received more than 1 transplant. 116 of 156 recipients had malignant disease. 100 of 156 patients had ablative conditioning. The incidence of PEF was 14.7%. A multivariate analysis shows that older age, poor risk and unrelated cord blood donor recipients are significantly associated with a risk of developing PEF with hazard ratios of 1.125 (1.051–1.205), 3.508 (1.502–8.191), and 5.080 (1.141–22.625), respectively. OS was significantly decreased in patients with PEF versus without PEF (hazard ratio = 4.84, 95% CI, 2.814–8.322, $p < 0.0001$). Furthermore, in a multivariate analysis, there was a significant decrease in OS associated with PEF, CMV status and poor risk status with hazard ratios of 3.296 (1.73–6.26), 1.89 (1.08–3.30) and 1.93 (1.12–3.3), respectively. **Conclusion:** These results demonstrate an almost 15% incidence of PEF in pediatric SCT recipients. Older, poor risk and UCB donor recipients may be at higher risk of developing PEF. PEF was associated with the most significant impact on overall mortality independent of other risk factors. Improved prevention and therapeutic strategies for development of PEF in post allo SCT recipients may potentially reduce mortality in the future.

215

HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) IN WISKOTT ALDRICH SYNDROME (WAS): A SINGLE CENTER EXPERIENCE IN 25 PATIENTS

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WAS is a rare X-linked disease characterized by eczema, microthrombocytopenia, recurrent infections, autoimmune complications and malignancies. The gene responsible for WAS has been identified and termed *WAS*P. Without a successful HSCT, the prognosis of classical WAS with a complete absence of WASP expression is poor. In this report we analyze the outcome of 25 pts transplanted in a single center in a developing country.

Material and Methods: Period: 04/92–02/07; age:1–14 ys-old(M:2 ys). Eight pts received bone marrow(BM) from HLA matched (5 pts) or mismatched family donors(3 pts). 17 pts received an unrelated cord blood(URD CB). Preparatory regimen: Busulfan(BU)16 mg/kg+Cyclophosphamide 120–200 mg/kg in 24 pts or BU8 mg/kg + Fludarabine 125 mg/m^2:1 pt. ATG(rabbit) was added to patients transplanted from unrelated donors or mismatched family donors. GVHD prophylaxis: Cyclosporine(Csa)+ MTX:16 pts; Csa + steroids:8 pts and Csa + MMF:1 pt. After 2005, all pts submitted to an URD CB transplantation, received Csa+MTX as GVHD prophylaxis if the TNC infused was $> 3.0 \times 10^*7$/kg. **Results:** 21 pts(84%) are alive between 100 – 4745 days (M:790 d) after HSCT. All pts survived more than 28 days and were evaluable for engraftment. Primary graft failure (PGF) occurred in 2 pts (both URD CB 4/6) and one pt was submitted to a successful 2nd transplant. Most pts tolerated the procedure very well. See table below for transplant related complications.23/25 pts were analyzed for chimerism (VNTR). 13 pts had a complete chimerism. Ten pts were mixed chimeras immediately after HSCT and, later on, 3 pts became full chimeras. Four pts had autoimmune complications after transplant: 3 pts had idiopathic thrombocytopenic purpura(ITP) and one pt had severe auto immune hemolytic anemia (AIHA). Frequent viral infections (CMV, EBV, adenovirus) occurred in pts submitted to URD CB transplants. 2/21 surviving pts have permanent sequels from neurological viral infections. **Conclusions:** The excellent survival in this group of pts confirms the efficacy of HSCT in this disease. Pts receiving HSCT from 4/6 URD CB have a lower survival. Reactivation of viral infections were frequent complications in our pts and should be monitored closely.

Post-transplant complications

	URD CB Compatibility: 6/6 or 5/6 N = 11 pts	URD CB Compatibility: 4/6 N = 6 pts	BM from matched family donors N = 5 pts	BM from mismatched family donors N = 3 pts
Graft failure	0	2	0	0
Acute GVHD grade III-IV	3/11	1/4	0	0
Chronic GVHD extensive	2/11	1/4	0	0
Mixed chimeras	3 pts	2 pts	2 pts	0
Auto immune complications	0	2 pts (ITP and AIHA)	1 pt (ITP)	1 pt (ITP)
Overall Survival	91%	66%	80%	100%
Causes of death	1 pt: D + 1825: bronchopneumonia + respiratory failure	2 pts: D + 34 : PGF+ fungal infection and D + 132 : C-GVHD + bacterial sepsis	1 pt:D + 62: CMV pneumonia (1992)	0

216

IRON OVERLOAD IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) PATIENTS

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Background: Iron can be a highly toxic molecule to cells and tissues when it interacts with oxygen and generates free radicals. Free iron, ferritin and transferrin saturation have been shown to increase acutely in HSCT patients, and high ferritin levels can persist for years following HSCT. The prevalence of iron overload has not been defined in this population, and currently, no management guidelines exist. We describe a group of pediatric HSCT patients who were diagnosed with iron overload after developing liver function abnormalities and/or hyper-ferritinemia. **Methods:** We performed a detailed retrospective review of patients identified as having iron overload following allogeneic HSCT performed between 2001–2007. We included a subset of patients with known

iron overload pre-HSCT who required aggressive iron management post-HSCT. Liver iron concentration (LIC), a surrogate of total body iron burden, was assessed by liver biopsy and/or magnetic reasonance imaging (T2* or R2 MRI). Abnormal LIC was defined as >1.5 mg iron/g dry liver tissue. **Results:** Patient characteristics are presented in Table 1. 7 out of the 11 patients identified were not previously known to have iron overload. The majority of these patients presented with elevations in liver transaminases as the primary sign of excess iron. Liver biopsy and/or MRI were used to diagnose iron overload, and in all cases MRI was the method used to assess the change in iron burden while patients were receiving therapy. Most patients were managed with phlebotomy (range: 4–10 cc/kg of blood removed every 2–4 weeks). Phlebotomy was effective in reducing iron burden as evidenced by normalization of transaminases and decrease in LIC and ferritin. One patient, managed with an oral iron chelator, did not have a reduction of overall iron burden. **Conclusions:** . Iron overload should be considered in HSCT patients presenting with abnormal transaminases and/or hyperferritinemia after transplant. MRI is a useful diagnostic tool and may obviate the need for invasive liver biopsy. Phlebotomy appears to be effective in reducing iron burden, however the safety and efficacy of chelators is not yet established. There is a need for prospective studies to define the prevalence of iron overload, establish guidelines for screening, and develop safe and effective therapies. As a result, we have initiated a prospective study using R2 MRI to determine the incidence and morbidity associated with iron overload in this patient population.

Characteristics of Patients With Iron Overload

Number	Diagnosis, Age	Type of HSCT	Condition Leading to Iron Overload Diagnosis	Managment of Iron Overload	LIC pre/post treatment (mg iron/g liver)	ALT max/min (u/L)	Ferritin max/min (ng/mL)
1	Relapsed ALL, 1 yo	MURD	Abnormal LFT's	Phlebotomy	7.3/4.0	254/38	2,896/449
2	PNH, 18 yo	MURD	Abnormal LFT's	Desferasirox	10.7/13.6	910/56	5,127/2,527
3	Relapsed ALL, 6 yo	MURD	Abnormal LFT's	Phlebotomy	5.1/1.9	404/57	4,071/796
4	Relapsed ALL, 10 yo	MURD	Abnormal LFT's	Phlebotomy	16.0/–	314/53	5,586/2,350
5	Sickle Cell Anemia, 9 yo	MRD	Abnormal LFT's	Phlebotomy planned	4.9/–	313/–	1,810/–
6	AML, 4 yo	MRD	Hyperferritinemia	Phlebotomy planned	5.1/–	70/–	1,938/–
7	ALL, 12 yo	4/6 Cord	Abnormal LFT's	Phlebotomy planned	13.0/–	209/–	3,645/–
8	Diamond-Blackfan Anemia, 9 yo	MRD	Chronic transfusion history	Phlebotomy	17.5/0.9	13/4	1,029/119
9	Aplastic Anemia, 6 yo	MRD	Chronic transfusion history	Phlebotomy	22.5/–	35/20	4,574/2,824
10	Beta-thalassemia, 8 yo	MRD	Chronic transfusion history	Phlebotomy	7.0/–	38/31	3,900/658
11	Beta-thalassemia, 7 yo	MRD	Chronic transfusion history	Phlebotomy planned	8.6/–	94/41	1,888/–

Abbreviations: PNH = Paroxysmal Nocturnal Hemoglobinuria, ALL = Acute Lymphoblastic Leukemia, AML = Acute Myeloid Leukemia, MURD = Matched Unrelated Donor, MRD = Matched Related Donor, ALT = Alanine Aminotransferase.

217

CHALLENGES IN THE USE OF HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR ECTODERMAL DYSPLASIA WITH IMMUNE DEFICIENCY

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Genetic mutations affecting regulatory proteins of NF-κB result in heritable diseases of development and immunity. Hypomorphic, X-linked mutations in the *IKBKG* gene (NEMO protein), and hypermorphic, autosomal dominant mutations in the *IKBA* gene (IκBα protein), are associated with a phenotype of ectodermal dysplasia with immune deficiency (ED-ID). ED-ID predisposes patients to bacterial and mycobacterial infections, and is typically fatal. Allogeneic HSCT may correct the immune deficiency associated with NEMO or IkBα mutations, but there are few reports. We report 3 patients with ED-ID who underwent HSCT. All patients experienced engraftment difficulties. Patient 1 presented with fevers, diarrhea, diffuse erythema and desquamation. Hypogammaglobulinemia with normal B- and T- cell numbers and subsets were noted, and genetic analysis revealed a hypomorphic NEMO mutation. He received matched sibling donor peripheral blood stem cells (PBSC) at 6 months following reduced-intensity conditioning with fludarabine, busulfan and ALG. Neutrophil engraftment was achieved at day +17, and maximal donor T-cell chimerism of 53% at day +77, which then declined. A second PBSCT from the same donor was undertaken after conditioning with alemtuzumab, fludarabine and melphalan, with stable donor chimerism through day +310. Patient 2 developed diarrhea, failure to thrive and recurrent infections including MAI. Inadequate antibody responses, but normal B- and T- cell numbers and subsets were noted. Genetic analysis demonstrated a hypomorphic NEMO mutation. A MUD BMT was performed at 3 years of age following myeloablative conditioning with busulfan, cyclophosphamide and ALG. Poor engraftment was noted, with persistent neutropenia despite chimerism of 95% donor at day +38. The patient was re-conditioned with fludarabine, and a CD34-selected PBSC boost from the same donor. Although complete chimerism was achieved, the patient remained pancytopenic and died at day +314 of gram-negative infection. Patient 3 presented with recurrent bacterial infections, p.carinii, and chronic diarrhea. Genetic analysis confirmed an IκBα mutation. The patient underwent a MUD cord blood transplant following myeloablative conditioning with busulfan and cyclophosphamide, but expired from sepsis prior to engraftment. These cases suggest that patients with immune deficiencies caused by NEMO or IκBα mutations may have intrinsic barriers to successful engraftment, which require further investigation.

218

LOWER LEUKEMIA RELAPSE IN PATIENTS WITH PULMONARY CYTOLYTIC THROMBI AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT

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Pulmonary cytolytic thrombi (PCT) is an uncommon post-transplant complication, which is more commonly reported in children than adults. PCT typically presents with low grade fever, cough, shortness of breath and/or hypoxia. Lung CT findings range from small, peripheral nodules to large diffuse infiltrates. The diagnosis is established by lung biopsy, which reveals areas of the pulmonary vasculature which are occluded with cellular debris. Bronchoscopy and lung biopsy are negative for infectious organisms by both immuno-stains and culture. While the pathogenesis of PCT is not currently known, it has been previously shown that patients with PCT frequently have concurrent aGVHD and that PCT responds to systemic corticosteroid treatment. Considering that such treatment may impair graft vs. leukemia (GVL) reactions, we investigated the outcome of patients who developed PCT after transplantation for hematological malignancy. From 1993–2006, we identified 14 pediatric patients with biopsy proven PCT and a hematological malignancy (9 ALL, 3 AML and 2 CML). PCT was diagnosed at an average of 90+/-38 days (range 38–342) after transplant. We compared outcomes to a cohort of pediatric leukemia patients that not develop PCT, but were transplanted during the same time interval (n = 323). There were no significant differences